

PTO/SB/08a (05-03)

Approved for use through 04/30/2003. OMB 0651-0031

U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for Form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 1 of 5

**Complete if Known**

Application Number	10/824,005
Filing Date	April 14, 2004
First Named Inventor	John H. GRIFFIN
Art Unit	1624
Examiner Name	Not yet assigned
Attorney Docket Number	P-082-US3

**U.S. PATENT DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code <sup>2</sup> (if known)			
KN ↓	A1	US- 5,397,787	03-14-1995	Buzzetti et al.	
	A2	US- 5,481,148	10-24-1995	Lewis et al.	
	A3	US- 5,521,184	05-28-1996	Zimmermann	
	A4	US- 5,593,991	01-14-1997	Adams et al.	
	A5	US- 5,593,992	01-14-1997	Adams et al.	
	A6	US- 5,670,527	09-23-1997	Adams et al.	
	A7	US- 5,945,418	08-31-1999	Bemis et al.	
	A8	US- 5,977,103	11-02-1999	Adams et al.	

**FOREIGN PATENT DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	7 <sup>6</sup>
		Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				
KN ↓	B1	WO 94/26260	11-24-1994	Yissum Research Dev. Company of Hebrew Univ		
	B2	WO 96/21452	07-18-1996	Smithkline Beecham Corp		
	B3	WO 96/33980	10-31-1996	Zeneca Limited		
	B4	WO 96/34867	11-07-1996	Warner-Lambert Co.		
	B5	WO 97/19065	05-29-1997	Celltech Therapeutics		
	B6	WO 97/40019	10-30-1997	Celltech Therapeutics		
	B7	WO 98/18782	05-07-1998	Celltech Therapeutics		
	B8	WO 98/37881	09-03-1998	Warner Lambert Co.		
	B9	WO 99/24442	05-20-1999	Ariad Pharmaceuticals		
	B10	WO 00/61578	10-19-2000	Sloan-Kettering Institute		

Examiner  
SignatureDate  
Considered

10/25/2004

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. 1 Applicant's unique citation designation number (optional). 2 See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. 3 Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). 4 For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. 5 Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. 6 Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 2 of 5

**Complete if Known**

Application Number	10/824,005
Filing Date	April 14, 2004
First Named Inventor	John H. GRIFFIN
Group Art Unit	1624
Examiner Name	Not yet assigned
Attorney Docket Number	P-082-US3

**OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
KM	C1	Adams et al., "Recent progress towards the identification of selective inhibitors of serine/threonine protein kinases", Current Opinion in Drug Discovery & Development, Vol. 2(2), pp 96-109 (1999)	
	C2	Ayyangar et al., "Anthraquinone and Anthrone Series-XXII/The Non-Identity of 1:3:8-Trihydroxy-2-Hydroxymethyl-Anthraquinone with Versicolorin and a Synthesis of Damnacanthal and Damnacanthol", Tetrahedron, Vol. 6, pp 331-337 (1959)	
	C3	Bajaj et al., "Improved Preparative Synthesis of Piceatannol (3,4,3',5'-Tetrahydroxy-Trans-Stilbene), Rev. Latinoamer Quim., Vol. 18(2), pp 79-80 (1987)	
	C4	Bit et al., "Inhibitors of Protein Kinase C. 3. Potent and Highly Selective Bisindolylmaleimides by Conformational Restriction", J. Med. Chem., Vol. 36, pp 21-29 (1993)	
	C5	Bullington et al., "The Development of Novel and Selective p56 <sup>lck</sup> Tyrosine Kinase Inhibitors", Bioorganic & Medicinal Chemistry Letters 8, pp 2489-2494 (1998)	
	C6	Bunin et al., "[26] Synthesis and Evaluation of 1,4-Benzodiazepine Libraries", Methods in Enzymology, Vol. 267, pp 448-465 (1996)	
	C7	Connolly et al., "Discovery and Structure-Activity Studies of a Novel Series of Pyrido[2,3-d]Pyrimidine Tyrosine Kinase Inhibitors", Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 18, pp 2415-2420 (1997)	
	C8	Duncia et al., "MEK Inhibitors: The Chemistry and Biological Activity of U0126, Its Analogs, and Cyclization Products", Bioorganic & Medicinal Chemistry Letters, Vol. 8, pp 2839-2844 (1998)	
	C9	Faltynek et al., "Damnacanthal Is a Highly Potent, Selective Inhibitor of p56 <sup>lck</sup> Tyrosine Kinase Activity", Biochemistry, Vol. 34, pp 12404-12410 (1995)	
	C10	Fry et al., "Specific, irreversible inactivation of the epidermal growth factor receptor and erbB2, by a new class of tyrosine kinase inhibitor", Proc. Natl. Acad. Sci. USA, Vol. 95, pp 12022-12027 (1998)	
	C11	Furet et al., "Structure-Based Design, Synthesis, and X-ray Crystallography of a High-Affinity Antagonist of the Grb2-SH2 Domain Containing an Asparagine Mimetic", J. Med. Chem., Vol. 42, pp 2358-2363 (1999)	

Examiner  
SignatureDate  
Considered

10/25/2004

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 3 of 5

**Complete if Known**

Application Number	10/824,005
Filing Date	April 14, 2004
First Named Inventor	John H. GRIFFIN
Group Art Unit	1624
Examiner Name	Not yet assigned
Attorney Docket Number	P-082-US3

**OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
KH	C12	Hamby et al., "Structure-Activity Relationships for a Novel Series of Pyrido[2,3-d]pyrimidine Tyrosine Kinase Inhibitors", J. Med. Chem. Vol. 40, pp 2296-2303 (1997)	
	C13	Hanefeld et al., "One-pot synthesis of tetrasubstituted pyrazoles-proof of regiochemistry", J. Chem. Soc., Perkin Trans. 1, pp 1545-1552 (1996)	
	C14	Hanke et al., "Discovery of a Novel, Potent, and Src Family-selective Tyrosine Kinase Inhibitor", The Journal of Biological Chemistry, Vol. 271, No. 2, Issue of January 12, pp 695-701 (1996)	
	C15	Henry et al., "Potent Inhibitors of the Map Kinase p38", Bioorganic & Medicinal Chemistry Letters 8, pp 3335-3340 (1998)	
	C16	Henry et al., "6-Amino-2-(4-fluorophenyl)-4-methoxy-3-(4-pyridyl)-1H-pyrrolo[2,3-b]pyridine (RWJ 68354): A Potent and Selective p38 Kinase Inhibitor", J. Med. Chem., Vol. 41, pp 4196-4198 (1998)	
	C17	Klutchko et al., "2-Substituted Aminopyrido[2,3-d]pyrimidin-7(8H)-ones. Structure-Activity Relationships Against Selected Tyrosine Kinases and in Vitro and in Vivo Anticancer Activity", J. Med. Chem. Vol. 41, pp 3276-3292 (1998)	
	C18	Lawrence et al., "Protein Kinase Inhibitors: The Tyrosine-Specific Protein Kinases", Pharmacol. Ther., Vol. 77, No. 2, pp 81-114 (1998)	
	C19	Levitzi et al., "Tyrosine Kinase Inhibition: An Approach to Drug Development", Science, Vol. 267, pp 1782-1788 (1995)	
	C20	Maly et al., "Combinatorial target-guided ligand assembly: Identification of potent subtype-selective c-Src inhibitors", PNAS, Vol. 97, No. 6, pp 2419-2424 (2000)	
	C21	Myers et al., "The Preparation and SAR of 4-(Anilino), 4-(Phenoxy), and 4-(Thiophenoxy)-Quinazolines: Inhibitors of p56 <sup>lck</sup> and EGF-R Tyrosine Kinase Activity", Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 4, pp 417-420 (1997)	
	C22	Proff et al., "Bivalent Inhibitors of Protein Tyrosine Kinases", J. Am. Chem. Soc., Vol. 121, pp 280-283 (1999)	

Examiner  
SignatureDate  
Considered

10/25/2004

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

4

of

5

**Complete if Known**

Application Number	10/824,005
Filing Date	April 14, 2004
First Named Inventor	John H. GRIFFIN
Group Art Unit	1624
Examiner Name	Not yet assigned
Attorney Docket Number	P-082-US3

**OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
KM	C23	Ramdas et al., "Benzodiazepine Compounds as Inhibitors of the Src Protein Tyrosine Kinase: Screening of a Combinatorial Library of 1,4-Benzodiazepines", Archives of Biochemistry and Biophysics, Vol. 368, No. 2, pp 394-400 (1999)	
	C24	Schoepfer et al., "Highly Potent Inhibitors of the Grb2-SH2 Domain", Bioorganic & Medicinal Chemistry Letters, Vol. 9, pp 221-226 (1999)	
	C25	Shibuya et al., "Syntheses of Two Pairs of Enantiomeric C18-Sphingosines and a Palmitoyl Analogue of Gaucher Spleen Glucocerebroside", Chem. Pharm. Bull., Vol. 40(5), pp 1154-1165 (1992)	
	C26	Smyth et al., "Non-Amine Based Analogues of Lavendustin A as Protein-Tyrosine Kinase Inhibitors", J. Med. Chem., Vol. 36, pp 3010-3014 (1993)	
	C27	Stover et al., "Recent advances in protein kinase inhibition: Current molecular scaffolds used for inhibitor synthesis", Current Opinion in Drug Discovery & Development, Vol. 2(4), pp 274-285 (1999)	
	C28	Sun et al., "Synthesis and Biological Evaluation of 3-Substituted Indolin-2-ones: A Novel Class of Tyrosine Kinase Inhibitors That Exhibit Selectivity toward Particular Receptor Tyrosine Kinases", J. Med. Chem., Vol. 41, pp 2588-2603 (1998)	
	C29	Tamaoki et al., "Staurosporine, A Potent Inhibitor of Phospholipid/Ca <sup>++</sup> Dependent Protein Kinase", Biochemical and Biophysical Research Communications, Vol. 135, No. 2, pp 397-402 (1986)	
	C30	Trumpf-Kallmeyer et al., "Development of a Binding Model to Protein Tyrosine Kinases for Substituted Pyrido[2,3-d]pyrimidine Inhibitors", J. Med. Chem., Vol. 41, pp 1752-1763 (1998)	
	C31	Vu et al., "Discovery of Potent and Selective SH2 Inhibitors of the Tyrosine Kinase ZAP-70", J. Med. Chem., Vol. 42, pp 4088-4098 (1999)	
	C32	Williams et al., "Ro 09-2210 Exhibits Potent Anti-proliferative Effects on Activated T Cells by Selectively Blocking MKK Activity", Biochemistry, Vol. 37, pp 9579-9585 (1998)	
	C33	Yao et al., "Potent Inhibition of Grb2 SH2 Domain Binding by Non-Phosphate-Containing Ligands", J. Med. Chem., Vol. 42, pp 25-35 (1999)	

Examiner  
SignatureDate  
Considered

10/25/2004

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet

5

of

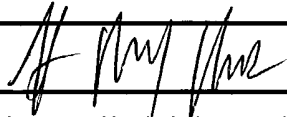
5

**Complete If Known**

Application Number	10/824,005
Filing Date	April 14, 2004
First Named Inventor	John H. GRIFFIN
Group Art Unit	1624
Examiner Name	Not yet assigned
Attorney Docket Number	P-082-US3

**OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
KM	C34	Zimmermann et al., "Phenylamino-Pyrimidine (PAP) Derivatives: A New Class of Potent and Selective Inhibitors of Protein Kinase C (PKC), Arch. Pharm. Pharm. Med. Chem., Vol. 329, pp 371-376 (1998)	

Examiner  
SignatureDate  
Considered

10/25/2004

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

1 Applicant's unique citation designation number (optional). 2 Applicant is to place a check mark here if English language Translation is attached. This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.